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Neurocognition, Insight into Illness and Subjective Quality-of-Life in Schizophrenia: What is Their Relationship?

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Abstract

Subjective quality-of-life (SQOL) has been recognized as a crucial domain of outcome in schizophrenia treatment, and yet its determinants are not well understood. In a recent meta-analytic investigation of 10 studies of neurocognition and SQOL in schizophrenia (Tolman & Kurtz, *Scz Bull*, in press) measures of crystallized verbal ability and processing speed were moderately negatively correlated with SQOL. One potential explanation for inverse relationships between measures of elementary neurocognition and SQOL is that higher levels of cognition may serve as a proxy for better insight into the illness, and better consequent recognition of illness-related functional impairment. This study sought to determine whether: (1) symptoms, neurocognitive variables, and insight into illness influence SQOL; and, (2) whether insight mediated or moderated a relationship between elementary neurocognitive function and SQOL. Seventy-one stabilized clients with schizophrenia or schizoaffective disorder were administered a neuropsychological test battery, symptom and subjective quality-of-life measures. Elementary neuropsychological measures of crystallized verbal ability, attention and working memory, and problem-solving were all inversely related to SQOL. Insight into illness and depression severity, but not positive and negative symptoms, were also inversely related to SQOL. Insight was not found to mediate or moderate any of the relationships between elementary neurocognition and SQOL. Taken together, these findings suggest that neurocognition and insight into illness have inverse relationships to SQOL and that elementary neurocognition does not influence SQOL through its link with illness insight.

Introduction

With the emergence of more effective pharmacologic management of acute psychiatric symptoms in schizophrenia, increasing attention has been paid to the development of interventions targeted at improving long-term functional and subjective outcomes for people

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Contributors

Matthew M. Kurtz, Ph.D., was responsible for initial conceptualization and design of the study (along with AWT), oversaw all data collection, conducted portions of the statistical analyses, formulated the data analytic plan, and co-wrote the manuscript.

Ari W. Tolman, B.A., was responsible for design of the study (along with MMK), conducted portions of the statistical analyses and co-wrote the manuscript.

Conflict of Interest

The authors report no conflicts-of-interest in the conduct or preparation of this study.

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with the illness, which remain poor for many clients. Objective measures of community function and quality-of-life (QOL), such as number and quality of social relationships, employment status and recreational engagement have most frequently been used as endpoints in studies of outcome schizophrenia (Green 1996; Green et al., 2000; Green et al., 2004). Although there is not a single definition of QOL, most agree that it is a multi-dimensional construct that includes not only objective components of community function, but subjective assessments of well-being as well (Test et al., 2005). Subjective assessment of well-being, however, has not traditionally been the focus of outcome studies in schizophrenia.

More recently, a growing emphasis in the schizophrenia literature has been placed the use of scales designed to assess the construct of subjective quality-of-life (SQOL) or life satisfaction (e.g., Test et al., 2005), particularly given its expressed importance by consumers. SQOL, according to this model, specifically refers to client satisfaction across life domains parallel to those typically assessed by measures of objective community function. For example, the domain of social relations might be measured in an objective scale by asking questions about the frequency of the patient's social contacts, e.g. "How often do you spend time with close friends?" In contrast, SQOL for social relations measures patient satisfaction, asking for a subjective assessment of quality of the client's interactions with others, e.g. "How do you feel about the amount of time you spend with other people?" (e.g., Lehman et al., 1988).

Despite the clear importance of SQOL as an outcome measure in studies of schizophrenia, along with the emergence of more refined tools for measuring SQOL, an understanding of factors that affect SQOL and how these factors interact in people with schizophrenia remains largely unexplored. An obvious candidate would be persistent, treatment refractory psychiatric symptoms. Studies evaluating psychiatric symptoms and SQOL have found associations between measures of depression and SQOL, but not positive and negative symptoms (e.g., Narvaez et al., 2008; Ruggeri et al., 2005).

One potential determinant of SQOL could be neurocognitive function. Individuals diagnosed with schizophrenia consistently show 1–2 SD deficits on measures of speed of processing, attention/vigilance, working memory, verbal learning and memory, visual learning and memory, reasoning and problem solving. Particular significance has been attached to these deficits as many have been moderately associated both cross-sectionally and longitudinally, with impaired community functioning and objective QOL in individuals with schizophrenia. Moreover, these deficits may actually better account for the diversity of community outcomes in schizophrenia than positive or negative symptoms (Green et al., 2000). The relationship of these deficits to SQOL, however, remains less well understood.

Studies of neurocognition and SQOL to date have been highly discordant, with some studies reporting no relationships between neurocognition and SQOL (Brissos et al. 2008; Chino et al., 2009; Hofer et al. 2005; Smith et al., 1999), others reporting negative relationships (Brekke et al, 2001; Corrigan & Buican, 1995; Dickerson et al. 1998; Narvaez et al, 2008), and still others reporting positive relationships (Alpetkin et al.; 2005; Herman, 2004). Differences between study findings may possibly be related to sample size and characteristics and /or neurocognitive and SQOL measures selected. In a recent meta-analytic investigation of studies of neurocognition and SQOL in schizophrenia (Tolman & Kurtz, in press) measures of crystallized verbal ability and processing speed were moderately negatively correlated with SQOL ($d=-.29$, and $d=-.19$, respectively), while verbal fluency was modestly and positively correlated ($d=.26$) with SQOL. These findings were not moderated by psychiatric symptoms. One potential explanation for inverse relationships between elementary neurocognition and SQOL is that higher levels of

cognition may serve as a proxy for improved insight into the illness, and improved insight in turn: (1) may lead to a better understanding of the chronic nature of the limitations that the disease may place on life function, leading to a poorer perceived quality-of-life, and (2) an internalization of social stigma regarding severe mental illness, also leading to poorer perceived SQOL.

To our knowledge, there have been no studies investigating the interrelationships of measures of psychiatric symptoms, elementary neurocognition, insight into illness and SQOL collected from the same sample of clients with schizophrenia and schizoaffective disorder. We sought to determine whether: (1) symptoms, neurocognitive variables, and insight into illness influence SQOL in schizophrenia, and then; (2) whether insight mediates the relationship between elementary neurocognitive function and SQOL; that is, does impaired cognitive function impair illness insight, which in turn influences SQOL. Alternatively, insight might moderate the relationship between neurocognition and SQOL. Thus we also assessed whether the relationship between elementary neurocognitive skills and SQOL was different at low, medium and high levels of illness insight. We predicted that: (1) consistent with previous work (e.g., Eack & Newhill, 2007; Narvaez et al., 2008) depressive symptoms, but not positive or negative symptoms, would predict lower levels of subjective QOL; (2) consistent with previous work, measures of elementary neurocognition would be inversely related to SQOL (Tolman & Kurtz, in press; Narvaez et al., 2008); (3) insight would be negatively related to SQOL, and (4) insight would mediate the relationship between elementary neurocognition and subjective quality of life.

Methods

Participants

Sixty-eight clinically stable, community-dwelling individuals and three long-term hospitalized inpatients with schizophrenia or schizoaffective disorder participated (n=71). Diagnosis was confirmed by the patient form of the Structured Clinical Interview for DSM-IV (SCID; First et al., 1996). Exclusion criteria for all potential participants were: (a) known neurological disease, (b) developmental disability, (c) current substance abuse, (d) mental retardation as evidenced by a history of services, or (e) lack of fluency in English. All patients provided written informed consent and all procedures met institutional ethical review. Data for this study were collected at entry to an ongoing study of the effects of cognitive remediation on cognitive and social dysfunction in people with schizophrenia (Kurtz et al., 2007). Clinical and demographic characteristics of the sample are presented in Table 1.

Assessment Measures

Symptom Assessment—The Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987) was used to assess symptoms. This measure is a semi-structured interview that generates ratings of signs and symptoms on 30, 7-point Likert scale items. Symptom raters for the study maintained interrater reliability through periodic rater training sessions, and all raters were trained to a criterion reliability of .8 intraclass correlation coefficient (ICC), across four jointly viewed, but independently-rated interviews. The subscales for total positive and total negative symptoms were selected as the independent measures.

Insight into Illness—Lack of Judgment and Insight from the PANSS; (Kay et al., 1987) was used to measure illness insight. The measure is a 7-point, clinician-rated item from the PANSS in which clients are rated from “1”, no impaired awareness or understanding of one’s own psychiatric condition and life situation, to a “7”, emphatic denial of past and present psychiatric illness.

Depression—Beck Depression Inventory (BDI; Beck, 1978): A 21-item multiple choice, self-report inventory that measures symptoms of depression such as hopelessness and irritability, cognitions such as guilt or feelings of being punished, and physical symptoms of fatigue, and weight loss.

Neuropsychological Assessment—All participants were administered a neuropsychological test battery including the vocabulary, digit span and digit symbol subtests from the Wechsler Adult Intelligence Scale-III or IV (WAIS-III and IV; Wechsler, 1997; 2008), Controlled Oral Word Fluency (FAS; Spreen & Strauss, 1998), California Verbal Learning Test (Delis et al., 2000), and the Penn Conditional Exclusion Test (PCET; Kurtz et al., 2004). For the CVLT, total score across the five learning trials was selected as the independent measure. For the PCET, the categories achieved score was selected for analysis. Measures were selected based on their relationships with functional status in previous studies of schizophrenia (e.g., Green et al., 2000; 2004).

Subjective Quality of Life—(SWL; Stein & Test 1980; Test et al., 2005): A 21-item self-report measure that targets subjective satisfaction with one's living situation, work, social contacts and psychological state.

Data Analysis

The Statistical Package for the Social Sciences (SPSS 15.0) was used for statistical analyses. Raw scores for each of the measures were converted to age -corrected z-scores using published normative data, with the exception of categories on the PCET for which normative data was not available. For this measure, z-scores were calculated from the client sample. The data analytic plan was conducted in two stages. In stage 1, Pearson's product-moment correlations were calculated between each of the neurocognitive variables, positive and negative symptom severity, measures of depression and insight into illness, and SQOL. In stage 2, a series of hierarchical regression models was tested using each of the neurocognitive measures that were correlated with SQOL in stage 1. In step 1, each measure of neurocognitive function linked to SQOL in stage 1 was entered. In step 2, insight was entered into the equation. This second step allowed us to both: (1) identify the unique contribution of insight to SQOL beyond elementary neurocognitive function, and (2) determine whether measures of insight mediated the relationship between elementary neurocognitive function and life satisfaction. If insight could be conceptualized as a construct predicting variance in life satisfaction separate from elementary neurocognitive function, we would expect a significant increase in explained variance when insight was added in step 2 of this regression, with the elementary neurocognitive domains remaining related to life satisfaction. Alternatively, if insight mediated the relationship between elementary neurocognition and life satisfaction, we would expect that, according to the methods of Baron & Kenny (1986): (1) insight would be related to life satisfaction, (b) elementary neurocognitive function would be related to life satisfaction, (c) insight into illness would be related to elementary neurocognitive function, and (d) when insight was controlled for statistically the relationship between the elementary neurocognitive variable and life satisfaction would be reduced or removed. In the third and final step of each regression, we entered the interaction term for the main effects of the elementary neurocognitive variable and the insight variable, to assess whether insight into illness moderated the relationship between elementary neurocognitive function and subjective life satisfaction. Procedures for assessing moderation in this manner are presented in Kraemer et al. (2002). All predictor variables in these regressions were centered around their mean to remove non -essential collinearity. All analyses were two-tailed and alpha was set at .05.

Results

Relationships Among the Study Variables

Correlations between standardized neuropsychological scores, positive and negative symptoms, depression, insight into illness, and satisfaction with life are presented in Table 2. Elementary neuropsychological measures, WAIS-Vocabulary ($r = -.37, p < .01$), Digit Span ($r = -.25, p < .05$), and PCET Categories ($r = -.25, p < .05$) were all inversely related to life satisfaction. Insight into illness ($r = -.34, p < .01$) and depression severity ($r = -.45, p < .01$) were also inversely related to life satisfaction. Crystallized verbal ability was related ($r = .42, p < .01$) to insight into illness.

Associations Between Elementary Neurocognitive Function, Insight into Illness and Satisfaction with Life

When the three elementary neurocognitive measure linked to satisfaction with life in the correlational analysis (WAIS-Vocabulary, Digit Span, and PCET categories) were entered first into a series of three hierarchical regressions, followed by insight, insight remained a significant predictor of SWL for regressions including Digit Span and PCET. In the regression with Digit Span, insight produced a significant change in R^2 (.10; $F[1,68]=8.45, p < .01$), and explained 10% of the variance of SWL scores beyond that associated with Digit Span (see Table 3, step 2). In the regression with PCET, insight produced a significant change in R^2 (.10; $F[1,67]=7.54, p < .01$), and explained 10 % of the variance of SWL scores beyond that associated with PCET categories (see Table 3, step 2). In the regression with Vocabulary, insight produced a change in R^2 (.04) that approached significance ($p = .063$; see Table 3, step 2).

Insight into Illness as a Mediator of the Relationship between Crystallized Verbal Ability and Life Satisfaction

The correlational analyses revealed the prerequisite relationships between insight into illness, SWL, and WAIS-Vocabulary for potential mediation. Mediation was tested with hierarchical regressions for this neurocognitive measure (see Table 3, step 3). In the regression, the relationship of crystallized verbal ability and life satisfaction remained significant when insight was added to the regression model. Because entering the insight into illness measure did not eliminate the relationship of WAIS-Vocabulary to SWL, the data suggests that insight into illness does not mediate the relationship between WAIS-Vocabulary and SWL. Prerequisite correlational relationships for mediation were not evident for any of the other elementary neurocognitive measures (see Table 2); consequently, no tests for mediation were conducted for those measures.

Insight as a Moderator of the Relationship Between Elementary Neurocognitive and Life Satisfaction

Results from the hierarchical regression analyses testing the moderating effects of insight into illness in the relationship between measures of neurocognition and life satisfaction found that the interaction term was not significant in the models for any of the neurocognitive measures (see Table 3).

Discussion

This is the first study, to our knowledge, to systematically analyze the role of symptoms, elementary neurocognitive deficits and insight into illness as predictors of SQOL in clients with schizophrenia. Our study revealed four main findings. First, consistent with hypothesis one, and previous studies, we found that severity of depression, but not positive or negative symptomatology, was positively related to subjective quality-of-life (e.g., Dickerson et al.,

1998; Narvaez et al., 2008; Aki et al., 2008). Second, also consistent with our hypotheses and previous literature (Eack & Newhill, 2007; Narvaez et al., 2008; Pyne et al., 2001; Tolman & Kurtz, in press), we found that three measures of elementary neurocognition, crystallized verbal ability, attention, and executive-function, were all inversely related to SQOL. Third, our results confirmed that illness insight was inversely related to SQOL. Fourth, the results revealed that the relationship between neurocognitive deficits and satisfaction with life was not mediated or moderated by a measure of insight into illness in individuals with schizophrenia. In the mediation analysis, when insight was added to the regression model, it did not diminish the effect of crystallized verbal ability on SQOL. In the moderation analysis, in no case did elementary neurocognitive measures have differential effects on SQOL at different levels of insight. Taken together, these findings suggest that measures of elementary neurocognition and insight are related to SQOL and the influence of neurocognition on SQOL is direct, and not through its well-documented link to insight into illness (Aleman et al., 2006). We note that results of the stepwise regression showed that insight into illness explained variance beyond that explained by attention and working memory (digit span) and executive function (PCET) but not crystallized verbal ability (WAIS-Vocabulary scores; see Table 3). These findings suggest that there is overlap in the variance in SQOL explained by measures of crystallized verbal IQ and our measure of illness insight.

The lack of mediation evident in these analyses was contrary to our hypotheses. Our findings instead suggest that neurocognition has a direct and inverse effect on subjective SQOL: a possible explanation is that greater levels of working memory, executive-function and verbal ability may permit individuals to better represent, manipulate and make inferences regarding information concerning their current status, and thus make better assessments about their own functional deficits relative to others. Individuals with stronger cognitive abilities may experience a heightened awareness of missing age-appropriate milestones, and such group comparisons would be expected to negatively impact SQOL. These clients may also internalize negative social stigma about severe mental illness more effectively than clients with more impaired cognition. These findings also suggest that while insight into illness does negatively impact SQOL, other factors play an important role in influencing SQOL in clients with schizophrenia.

The inverse relationships between elementary neurocognition and insight into illness and SQOL found in this study underscore a potential tension between outcome goals in the treatment of schizophrenia. Today, many clinicians and researchers have a simultaneous interest in improving subjective and objective measures of well-being, as well as improving cognition and insight. Researchers and clinicians have turned towards therapies aimed at improving : (1) cognition for people with schizophrenia as research has linked neurocognitive deficits with impaired community functioning and objective QOL (e.g., living or vocational status) in individuals with schizophrenia, both cross-sectionally and longitudinally (Green et al. 2000, Green et al. 2004), and (2) illness insight as poor insight has been linked to reduced treatment adherence and increased hospitalizations (see Lysaker et al., 2009 for a review). The results of the current study raise questions regarding the assumption that improvement in subjective well-being will necessarily follow from improvement in cognition and/or insight as a function of treatment interventions. In fact, the current study suggests that there could be a paradoxical effect of treatment gains in cognition and/or insight leading to poorer SQOL. As the balance of current data suggests that evidence-based psychoeducational and cognitive remediation programs do improve aspects of objective QOL, the findings presented here might suggest that clinicians and researchers working with people with schizophrenia may have to develop tailored adjunctive interventions administered alongside these evidence-based therapies that are able to attend to the subjective well-being of clients.

Several caveats to the current study should be mentioned. First, this study had a cross-sectional study design and therefore we were unable to determine whether changes in cognition or insight over time are associated changes in life satisfaction. Longitudinal study design will be necessary to help elucidate any potential causal-effect between neurocognition, illness insight, and subjective life satisfaction. Second, we selected the “Lack of Judgment and Insight” item on the PANSS, as our measure of insight into illness. Follow-up studies might consider using other scales, such as the Scale to Assess Unawareness of Mental Disorder (SUMD; Amador et al., 1993), which provides a more comprehensive assessment that may better capture the multi-dimensional aspects of illness insight (Smith et al., 2000). Third, given the exploratory nature of our study, along with a moderate sample size, we did not correct for multiple comparisons and consequently the risk for Type I error was elevated. Fourth, in order to minimize the number of statistical comparisons, we did not formally evaluate demographic factors, including factors (e.g., duration of illness, gender) that have been linked to SQOL in previous studies of schizophrenia (e.g., Caron et al., 2005) and may play an additional role in understanding the links between symptoms, elementary neurocognitive function, illness insight and SQOL.

In summary, elementary neuropsychological measures of crystallized verbal ability, attention and working memory, and problem-solving were all inversely related to SQOL. Insight into illness and depression severity but not positive and negative symptoms, were also inversely related to SQOL. Insight was not found to mediate or moderate any of the relationships between elementary neurocognition and SQOL. These findings suggest that neurocognition and insight into illness have inverse relationships to SQOL and that elementary neurocognition does not influence SQOL through its link with illness insight.

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Table 1

Demographic and clinical characteristics of overall sample (n=71)

| Variable | Mean (SD; range) |
|--------------------------|--------------------|
| Age | 30.6 (10.8; 19–55) |
| Sex (% male) | 74.6 |
| Education | 12.4 (2.0; 8–18) |
| # of Hospitalizations | 4.9 (4.1; 0–20) |
| Illness Duration (years) | 9.5 (9.7; .5–37) |
| Depression (BDI) | 18.55 (12.8; 0–54) |
| PANSS Positive | 17.7 (5.6; 8–32) |
| PANSS Negative | 18.8 (5.4; 7–32) |

Note: SD: standard deviation; PANSS=Positive and Negative Syndrome Scale; BDI=Beck Depression Inventory.

Table 2

Intercorrelations of variables (n=71)

| Measure | 1. WAIS Vocab | 2. LFI | 3. Digit Span | 4. CVLT | 5. PCET | 6. Symbol-Digit | 7. PANSS-Judgement | 8. Positive | 9. Negative | 10. BDI |
|-------------------|---------------|--------|---------------|---------|---------|-----------------|--------------------|-------------|-------------|---------|
| Neurocognitive | | | | | | | | | | |
| 1. WAIS Vocab. | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- |
| 2. LFI | .01 | -- | -- | -- | -- | -- | -- | -- | -- | -- |
| 3. Digit Span | .28* | .19 | -- | -- | -- | -- | -- | -- | -- | -- |
| 4. CVLT | .20 | .12 | .33** | -- | -- | -- | -- | -- | -- | -- |
| 5. PCET | .31** | -.09 | .27* | .12 | -- | -- | -- | -- | -- | -- |
| 6. Symbol-Digit | .19 | .37** | .27* | .24* | .10 | -- | -- | -- | -- | -- |
| Insight/ | | | | | | | | | | |
| 7. PANSS-Judgment | .42** | .01 | .09 | .10 | .19 | -.02 | -- | -- | -- | -- |
| Symptom Severity | | | | | | | | | | |
| 8. Positive | .01 | .19 | -.01 | -.13 | -.21 | .25* | .25* | -- | -- | -- |
| 9. Negative | -.22 | -.16 | -.18 | .02 | -.35** | .32** | .04 | -- | -- | -- |
| 10. BDI | -.03 | -.01 | .01 | .05 | -.08 | -.25* | .08 | .25* | .10 | -- |
| Subjective QOL | | | | | | | | | | |
| 11. SWL | -.37** | -.14 | -.25* | -.23 | -.25* | -.13 | -.34** | -.04 | .16 | -.45** |

Note: BDI=Beck Depression Inventory; CVLT-II: California Verbal Learning Test-II; LFI=Letter Fluency PCET; Penn Conditional Exclusion Test; SWL=Satisfaction with Life; WAIS: Wechsler Adult Intelligence Scale.

* p≤.05.

** p≤.01

/ Scores have been multiplied by -1 such that higher scores reflect greater insight into illness.

Table 3

Multiple regressions for the prediction of subjective life satisfaction (SWL) by each elementary neurocognitive measure, insight (as measured by the judgment item of the PANSS), and the interaction of each neurocognitive measure and insight

| Measure | Step 1 Standardized beta | Step 2 Standardized beta | Step 3 Standardized beta | F- | R ² | R ² -change |
|-------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------|----------------|------------------------|
| <u>Vocabulary</u> | | | | | | |
| WAIS-Vocabulary | -.37 p=.002 | -.28 p=.026 | -.27 p=.033 | 10.90 p=.002 | .14 | – |
| Insight | | -.23 p=.063 | -.23 p=.069 | 7.44 p=.001 | .18 | .04 p=.063 |
| WAIS-VocabularyxInsight | | | -.03 p=.815 | 4.91 p=.004 | .19 | .00 p=.815 |
| <u>Digit Span</u> | | | | | | |
| Digit Span | -.21 p=.023 | -.19 p=.033 | -.20 p=.098 | 4.39 p=.040 | .06 | – |
| Insight | | -.16 p=.055 | -.15 p=.056 | 6.66 p=.002 | .16 | .10 p=.005 |
| DSxInsight | | | -.08 p=.078 | 4.80 p=.004 | .18 | .01 p=.305 |
| <u>PCET</u> | | | | | | |
| PCET | -.25 p=.038 | -.19 p=.100 | -.19 p=.091 | 4.49 p=.038 | .06 | – |
| Insight | | -.31 p=.008 | -.31 p=.007 | 6.23 p=.003 | .16 | .10 p=.008 |
| PCETxInsight | | | -.16 p=.149 | 4.94 p=.004 | .18 | .03 p=.149 |

Note: BDI: Beck Depression Inventory; PANSS: Positive and Negative Syndrome Scale; PCET: Penn Conditional Exclusion Test; SWL: Satisfaction with Life Scale; WAIS: Wechsler Adult Intelligence Scale.